Remarks

Reconsideration of this Application is respectfully requested.

I. Status of the Claims

Upon entry of the foregoing amendment, claims 143-146, 148-158, and 161-171 are pending in the application, with claims 143 and 144 being the independent claims.

II. The Claim Amendments

Claims 143-146, 148-158 and 161-171 are amended to recite "genetically glycoengineered." Support for this amendment is found, *inter alia*, at page 7, lines 24-25 of the specification as filed. Claim 168 is amended to recite "bisected, complex." Support for this amendment is found, *inter alia*, at page 37, lines 19-21 of the specification as filed. Claim 147 is canceled without prejudice to or disclaimer of the subject matter therein. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendments and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

III. The Office Action

A. Claim to Priority

At page 2 of the Office Action, the Examiner asserts that the disclosure of Application No. 09/294,584, to which the captioned application claims benefit, fails to provide adequate support for one or more claims under 35 U.S.C. § 112, 1st Paragraph. Applicants respectfully disagree. For reasons detailed in the following section regarding the New Matter rejection under 35 U.S.C. § 112, 1st Paragraph, Applicants submit that the present claims are fully supported by U.S. Application No. 09/294,584 and by U.S.

Provisional Application No. 60/082,581 ("the Priority Document"), of which the subject application also claims benefit, and which was incorporated by reference into the subject application.

B. Rejections Under 35 U.S.C. § 112, 1st Paragraph

Claims 143-158 and 168-171 have been rejected under 35 U.S.C. § 112, 1st Paragraph, as allegedly failing to comply with the written description requirement on the ground that the claims contain new matter. Office Action at pages 3-4. Applicants respectfully traverse this rejection. Specifically, the Examiner asserts that there is no literal support for the term "proportion of nonfucosylated oligosaccharides," and that the specification does not inherently support this limitation. Office Action at page 6. Applicants respectfully disagree with these assertions.

First, the Examiner is using an improper standard to conclude that there is no literal support for the claims. Namely, the Examiner states that "[n]on-fucosylated oligosaccharides are only mentioned once," Office Action at page 4, and that, "... the original claims did not mention 'an increased proportion of nonfucosylated oligosaccharides'; a search of the instant specification does not reveal the term 'nonfucosylated.'" Office Action at page 6. However, there is no requirement that, to satisfy the written description provisions, a minimum amount of disclosure must be devoted to a particular claim limitation. *See, e.g., Falkner v. Inglis*, 448 F.3d 1357 (Fed. Cir. 2006) ("No length requirement exists for a disclosure to adequately describe an invention.") (citing *In re Hayes Microcomputer Prods., Inc. Patent Litig.*, 982 F.2d 1527, 1534 (Fed. Cir. 1992) ("[T]he adequacy of the description of an invention depends on its content in relation to the particular invention, not its length.")).

Likewise, it is well-settled that *ipsis verbis* disclosure is not necessary to satisfy the written description requirement. *See, e.g., Eiselstein v. Frank*, 52 F.3d 1035, 1038 (Fed. Cir. 1995) ("In order to determine whether a prior application meets the 'written description' requirement with respect to later-filed claims, the prior application need not describe the claimed subject matter in exactly the same terms as used in the claims; it must simply indicate to persons skilled in the art that as of the earlier date the applicant had invented what is now claimed.") (citing *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563 (Fed. Cir. 1991) and *In re Wertheim*, 541 F.2d 257, 265 (CCPA 1976)); s*ee also*, *University of Rochester v. G.D. Searle & Co., Inc.*, 358 F.3d 916, 922-23 (Fed. Cir. 2004), *cert. denied*, 543 U.S. 1015 (2004) ("this court and its predecessor have repeatedly held that claimed subject matter 'need not be described in haec verba' in the specification to satisfy the written description requirement...").

Second, as discussed in Applicants' previous replies, the specification as filed--as well as the priority document of which it claims benefit--provides ample support for the claims. For example, explicit support for the term "increased proportion of nonfucosylated oligosaccharides" is found in the specification as filed at page 37, line 31 to page 38, line 6. There, it is stated that, "[h]igher accumulation of non-fucosylated (m/z 1664) bisected hybrid by-products, instead of fucosylated ones (m/z 1810), would agree with the fact that oligosaccharides which are first modified by GnT III can no longer be biosynthetic substrates for core α1,6-fucosyltransferase. Schachter, 1986, *Biochem. Cell Biol.* 64:163-181." Specification at page 38, lines 2-6. Although the Examiner contends that this statement is made only in reference to a specific example (see Office Action at page 4), it is clear from context that the principle is generally applicable. As previously mentioned, this was well-known in the field at the time of the

invention. For example, Schachter *et al.* in Figure 3 and the Priority Document explicitly state that "[t]he addition of fucose to the core of oligosaccharides can take place at any point after reaction 5 of the [central reaction network of the N-linked glycosylation pathway], ***but it is also blocked by the modifications that GalT or GnTIII introduce.***" *See* Schachter *et al., Biochem. Cell Biol. 64*:163-181 (1986) and Priority Document at page 17, lines 28-30. Thus, the Priority Document also identifies a relationship between GnT III expression and a reduction in core fucosylation. If the core fucosyltransferase cannot add a fucose residue to the core oligosaccharide structure, there will be an increased proportion of nonfucosylated oligosaccharides. GnTIII overexpression, therefore, necessarily results in decreased fucosylation (*i.e.*, increased nonfucosylation).

Support for the claims--in particular, the term "increased proportion of nonfucosylated oligosaccharides--is also found in the Figures as filed. For example, Figure 9, panels A-E, provide support for an increased proportion of nonfucosylated oligosaccharides.[1] This is evident from the fact that the peaks of nonfucosylated oligosaccharides (e.g., 1339, 1543, 1664, 1705, and 1867) change in height with changes in expression of GnTIII. Figure 15 also provides support for the term "increased proportion of nonfucosylated oligosaccharides." The antibody produced at the highest levels of GnTIII expression (C2B8-25t), would also have the highest number of bisected GlcNAc residues. Accordingly, as explicitly stated in the specification, there would be fewer fucosylated oligosaccharides (*i.e.*, an increased proportion of nonfucosylated oligosaccharides) because such glycan structures "could no longer be biosynthetic

[1] It is unclear why, at page 6 of the Office Action, the Examiner states that "there are no figures 9A-E in the specification as filed as applicants assert." Figure 9 has five panels labeled "A" to "E" at the upper left hand corner of each panel. Indeed, at page 4 of the Office Action, the Examiner himself refers to "Fig. 9C and D."

substrates for core α 1,6-fucosyltransferase." *See* Specification at page 38, lines 2-6 (citing Schachter 1986, *Biochem. Cell Biol.* 64:163-181). This antibody also had the highest levels of ADCC. Specification at Figure 15 and page 42, line 32 to page 43, line 18. Hence, the figures provide explicit support for the claims.

Third, the Examiner has twice acknowledged in the Office Action that increased expression of GnTIII necessarily leads to increased bisecting GlcNAc and reduced fucosylation. Office Action at pages 9 and 10. Indeed, at page 10 of the Office Action, the Examiner states that PCT Publication No. WO 99/54342 (Umaña *et al.*), which has ***the same specification as the instant application***, discloses that "[a]ntibodies produced in CHO-GnTIII cells had a glycosylation pattern ***with fewer fucosylated glycans*** and increased bisected glycans (both complex and hybrid) relative to Sp2/0 and CHO cells not expressing GnTIII. ***The change in glycosylation was linked to an increase in ADCC*** (see pages 35-39 and Figures 9-11) ... ." Office Action at page 10 (emphasis added). Clearly, if a reference with the same specification discloses that an antibody from a glycoengineered CHO cell has fewer fucosylated glycans relative to an antibody from non-glycoengineered cells, then that specification necessarily discloses an antibody with an increased proportion of nonfucosylated oligosaccharides compared to a non-glycoengineered antibody. To say otherwise would defy logic. Hence, the claims, including the term "increased proportion of nonfucosylated oligosaccharides," are fully supported by the specification and do not constitute new matter.

Regarding claim 168, the Examiner asserts that "there is no disclosure, either literal or inherent, of antibodies having only up to about 50% complex oligosaccharides" and that "the remaining 50% of the glycans would have to be either high-mannose or hybrid glycans. There is no disclosure of such a high percentage of high mannose or

hybrid glycans in the disclosed antibodies. What is disclosed is that up to 50% of the oligosaccharides may be bisected, complex glycans." Office Action at page 5. Applicants respectfully disagree that there is no disclosure for antibodies having only up to about 50% complex oligosaccharides. Nevertheless, solely in an effort to facilitate prosecution and not in acquiescence to the Examiner's rejection, claim 168 has been amended to recite "50% bisected, complex." Therefore, the rejection of claim 168 is thereby rendered moot.

For the reasons stated above, Applicants submit that the claims are fully supported by the specification as filed and are entitled to their earliest priority date. Accordingly, the rejection under 35 U.S.C. § 112, first paragraph, should be reconsidered and withdrawn.

C. Rejection Under 35 U.S.C. § 112, 2nd Paragraph

Claim 147 has been rejected under 35 U.S.C. § 112, 2nd Paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Office Action at page 7. Claim 147 has been canceled without prejudice to or disclaimer of the subject matter therein. Accordingly, the rejection is rendered moot and should be withdrawn.

D. Rejection Under 35 U.S.C. § 102

Claims 143-145, 147-155, 157, 158, 161-167, and 169-171 have been rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Nakamura *et al.*, *Cancer Res.* 54: 1511-1516 (1994), as evidenced by Shinkawa *et al.*, and Raju *et al.* Applicants respectfully traverse this rejection. The amended claims are directed to a "genetically glycoengineered recombinant antibody." Nakamura *et al.* do not teach or describe a genetically glycoengineered recombinant antibody. Therefore, the claims are not

anticipated by Nakamura *et al.* Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 102(b) be reconsidered and withdrawn.

Claims 143-158, 161-167 and 169-171 have been rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Umaña *et al.*, PCT Publication No. WO 99/54342. Applicants respectfully traverse this rejection. As discussed in detail above, the claims are fully supported by the specification as filed and are entitled to their earliest priority date. Hence, PCT Publication No. WO 99/54342 is not prior art against the claims and cannot anticipate the claims. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 102(b) be reconsidered and withdrawn.

E. Rejection for Obviousness-Type Double Patenting

Claims 143-147, 149-155, 157, 158, 161, 162, 164-167, and 169-171 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting over claims of copending Application No. 11/348,526. Applicants request that the rejection be held in abeyance until otherwise allowable claims are identified.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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